Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 4 of 34

## **AMENDMENTS TO THE CLAIMS:**

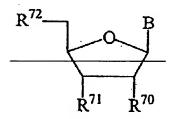
This listing of claims will replace all prior versions, and listings, of claims in the application.

## **LISTING OF CLAIMS:**

Claims 1-69 (canceled)

Claim 70 (currently amended): A labeled nucleoside/tide or nucleoside/tide analog emprising a rhodamine dye conjugated by a linker (L') to a nucleoside/tide or nucleoside/tide analog (NUC), wherein:

the rhodamine is a rhodamine-type parent xanthene having attached to the xanthene C9 carbon a phenyl group that is further substituted with an ortho carboxy or ortho sulfonate group or a salt thereof, one to three substituted or unsubstituted aminopyridinium groups and a substituted or unsubstituted alkylthio, or arylthio group; and the nucleoside/tide or nucleoside/tide analog and linker taken together comprise[[s]] the structure:



Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 5 of 34

## wherein:

B is a nucleobase selected from a purine, a 7-deazapurine, an 8-aza,7-deazapurine, a pyrimidine, a normal nucleobase and a common analog of a normal nucleobase;

## L' is the linker;

R<sup>70</sup> and R<sup>71</sup>, when taken alone, are each independently selected from hydrogen, hydroxyl and a moiety which blocks polymerase-mediated template-directed polymerization, or when taken together form a bond such that the illustrated sugar is 2',3'-didehydroribose; and

R<sup>72</sup> is selected from hydroxyl, a phosphate ester having the formula:

where a is an integer from 0 to 2, and a phosphate ester analog, or a salt thereof.

Claim 71 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 70 comprising the formula:

$$R^{24}$$
 $R^{24}$ 
 $R^{25}$ 
 $R^{26}$ 
 $R^{26}$ 

wherein:

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 6 of 34

Y is a rhodamine-type parent xanthene ring attached to the illustrated phenyl group at the xanthene C9 carbon;

 $R^{22}$ ,  $R^{23}$ ,  $R^{25}$ , and  $R^{26}$  are independently selected from hydrogen and (C<sub>1</sub>-C<sub>6</sub>) alkyl;

 $R^{24}$ , when taken alone, is  $(C_1-C_6)$  alkyl, or when taken together with  $R^{24}$  is  $(C_4-C_{10})$  alkyldiyl,  $(C_4-C_6)$  alkyleno,  $(C_4-C_6)$  heteroalkyldiyl and  $(C_4-C_6)$  heteroalkyleno;

 $R^{24}$ , when taken alone, is  $(C_1-C_6)$  alkyl, or when taken together with  $R^{24}$  is  $(C_4-C_{10})$  alkyldiyl,  $(C_4-C_6)$  alkyleno,  $(C_4-C_6)$  heteroalkyldiyl and  $(C_4-C_6)$  heteroalkyleno;

n is 1, 2, or 3;

S is sulfur;

 $Z^1$  is selected from (C<sub>1</sub>-C<sub>12</sub>) alkyldiyl, (C<sub>1</sub>-C<sub>12</sub>) alkyldiyl independently substituted with one or more of the same or different W<sup>1</sup> groups, (C<sub>5</sub>-C<sub>14</sub>) aryldiyl, and (C<sub>5</sub>-C<sub>14</sub>) aryldiyl independently substituted with one or more of the same or different W<sup>2</sup> groups;

 $W^1$  is selected from -X, -R, =O, -OR, -SR, =S, -NRR, =NR,  $-CX_3$ , -CN, -OCN, -SCN, -NCO, -NCS, -NO, -N

 $-SCN, -NCO, -NCS, -NO, -NO_2, =N_2, -N_3, -S(O)_2O^{-}, -S(O)_2OH, -S(O)_2R, -C(O)R,$ 

 $-C(O)X, -C(S)R, -C(S)X, -C(O)OR, -C(O)O^{-}, -C(S)OR, -C(O)SR, -C(S)SR,$ 

-C(O)NRR, -C(S)NRR AND -C(NR)NRR;

 $W^2$  is selected from -R, -OR, -SR, -NRR,  $-S(O)_2O^2$ ,  $-S(O)_2OH$ ,  $-S(O)_2R$ ,

 $-C(O)R, -C(O)X, -C(S)R, -C(S)X, -C(O)OR, -C(O)O^{-}, -C(S)OR, -C(O)SR, -C(S)SR, -C$ 

-C(O)NRR, -C(S)NRR and -C(NR)NRR;

L is a selected from a bond,  $(C_1-C_{12})$  alkyldiyl,  $(C_1-C_{12})$  substituted alkyldiyl,  $(C_6-C_{26})$  arylalkyldiyl, -O-, -S-, -NR-, -C(O)O-, -C(O)NR-,  $-NRS(O)_2-$ , -NR-NR-, -NRC(O)O-, and -NRC(O)NR-;

R<sup>46</sup> is selected from -C(O)NR-, -C(O)O-, and -C(O)S-,

L' is selected from  $(C_1-C_{20})$  alkyldiyl,  $(C_1-C_{20})$  heteroalkyldiyl,  $(C_1-C_{20})$  alkyleno,  $(C_1-C_{20})$  heteroalkyleno,  $(C_6-C_{26})$  arylalkyldiyl,  $(C_5-C_{20})$  heteroarylalkyldiyl, and substituted forms thereof; and

NUC is a nucleoside/tide or nucleoside/tide analog;

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 7 of 34

each R is independently selected from hydrogen,  $(C_1-C_6)$  alkyl,  $(C_5-C_{20})$  aryl,  $(C_6-C_{26})$  arylalkyl, and  $(C_5-C_{20})$  arylaryl; or when two R groups on the same nitrogen atom are taken together, those two R groups are  $(C_4-C_{10})$  alkyldiyl or  $(C_4-C_{10})$  alkyleno; and each X is independently a halogen.

Claim 72 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 71 wherein Y comprises the rhodamine-type parent xanthene ring structures:

$$(Y-1) \qquad \begin{array}{c} R^{6'} & R^{5} & R^{4} & R^{3} \\ R^{6} & R^{5} & R^{5} & R^{4} & R^{3} \\ R^{6} & R^{5} & R^{5} & R^{6} & R^{3} \\ R^{7} & R^{7} & R^{7} & R^{2} \end{array},$$

$$(Y-2) \quad R^{13} = R^{15} = R^$$

,

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 8 of 34

$$(Y-3) \qquad \begin{array}{c} R^{15} & R^{6} & R^{5} & R^{4} & R^{3} \\ R^{15} & N & O & P^{4} & R^{17} \\ R^{17} & R^{18} & R^{9} & R^{1} & P^{17} \end{array}$$

, and

and a salt thereof, wherein:

R<sup>1</sup> and R<sup>2</sup> when taken alone, are independently hydrogen or (C<sub>1</sub>-C<sub>6</sub>) alkyl;

 $R^3$  and  $R^3$ ' when taken alone, are independently selected from hydrogen, (C<sub>1</sub>-C<sub>6</sub>) alkyl, (C<sub>5</sub>-C<sub>14</sub>) aryl and (C<sub>5</sub>-C<sub>14</sub>) arylaryl, or when taken together is (C<sub>4</sub>-C<sub>6</sub>) alkyldiyl or (C<sub>4</sub>-C<sub>6</sub>) alkyleno, or when individually taken together with  $R^2$  or  $R^4$  is (C<sub>2</sub>-C<sub>6</sub>) alkyldiyl or (C<sub>2</sub>-C<sub>6</sub>) alkyleno;

 $R^4$ , when taken alone, is selected from hydrogen an  $(C_1-C_6)$  alkyl, or when taken together with  $R^3$  or  $R^3$  is  $(C_2-C_6)$  alkyldiyl or  $(C_2-C_6)$  alkyleno;

 $R^5$ , when taken alone, is selected from hydrogen and  $(C_1-C_6)$  alkyl, or when taken together with  $R^6$  or  $R^{6'}$  is  $(C_2-C_6)$  alkyldiyl or  $(C_2-C_6)$  alkyleno;

 $R^6$  and  $R^6$  when taken alone, are selected from hydrogen,  $(C_1-C_6)$  alkyl,  $(C_5-C_{14})$  aryl and arylaryl, or when taken together are  $(C_4-C_6)$  alkyldiyl or alkyleno, or when individually taken together with  $R^5$  or  $R^7$  is  $(C_2-C_6)$  alkyldiyl or alkyleno;

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 9 of 34

 $R^7$ , when taken alone, is selected from hydrogen and  $(C_1-C_6)$  alkyl, or when taken together with  $R^6$  or  $R^6$  is  $(C_2-C_6)$  alkyldiyl or alkyleno;

R<sup>8</sup>, when taken alone, is selected from hydrogen and (C<sub>1</sub>-C<sub>6</sub>) alkyl;

 $R^{10}$ ,  $R^{11}$ ,  $R^{12}$ ,  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$ ,  $R^{16}$ ,  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are each independently selected from hydrogen and (C<sub>1</sub>-C<sub>6</sub>) alkyl, or

when R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> taken together are (C<sub>5</sub>-C<sub>14</sub>) aryleno or (C<sub>5</sub>-C<sub>14</sub>) aryleno substituted with one or more of the same or different (C<sub>1</sub>-C<sub>6</sub>) alkyl, or when R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup> and R<sup>21</sup> taken together are (C<sub>5</sub>-C<sub>14</sub>) aryleno or aryleno substituted with one or more of the same or different (C<sub>1</sub>-C<sub>6</sub>) alkyl; and R<sup>9</sup> is the point of attachment to the xanthene C9 carbon.

Claim 73 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 72 wherein  $R^2$  when taken together with  $R^3$  or  $R^3$  is  $(C_2-C_6)$  alkyldiyl or  $(C_2-C_6)$  alkyleno.

Claim 74 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 72 wherein:

an alkyldiyl or alkyleno bridge formed by taking R<sup>2</sup> together with R<sup>3</sup> or R<sup>3</sup>, R<sup>7</sup> together with R<sup>6</sup> or R<sup>6</sup>, or R<sup>4</sup> together with R<sup>3</sup> or R<sup>3</sup>, is ethano, propano, 1,1-dimethylenopano or 1,1,3-trimethylpropano;

an aryleno bridge formed by taking R<sup>1</sup> together with R<sup>2</sup> is benzo or naphtho; an alkyldiyl or alkyleno bridge formed by taking R<sup>3</sup> together with R<sup>3</sup>, or R<sup>6</sup> together with R<sup>6</sup>, is butano;

an alkyldiyl or alkyleno bridge formed by taking R<sup>5</sup> together with R<sup>6</sup> or R<sup>6</sup>; is ethano, propano, 1,1-dimethylethano, 1,1-dimethylpropano and 1,1,3-trimethylpropano; and

an aryleno bridge formed by taking  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  together, or  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  together, is benzo.

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 10 of 34

Claim 75 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 71 in which  $Z^1$  is phenyldiyl.

Claim 76 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 71 in which L' is selected from: —C=C-CH<sub>2</sub>—and —C=C-CH<sub>2</sub>—O-CH<sub>2</sub>CH<sub>2</sub>—

Claim 77 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog

of Claim 71 in which L' is:  $-C \equiv C - CH_2 - O - CH_2CH_2 - N - R^{48} - W$  wherein  $R^{47}$  is hydrogen or  $(C_1 - C_6)$  alkyl, and  $R^{48}$  is selected from:

wherein each r is independently an integer from 1 to 6;  $R^{49}$  is hydrogen, (C<sub>1</sub>-C<sub>6</sub>) alkyl, or an amino acid side chain; and  $\phi$  is phenyldiyl or substituted phenyldiyl.

Claim 78 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 71 in which Y is selected from the structures:

January 13, 2004 Page 11 of 34

$$(Y-22a) \qquad \qquad H_2N \qquad \qquad N^{\oplus}$$

$$(Y-23a) \qquad H_2N \qquad Q \qquad N^{\Theta}$$

Page 12 of 34

Applicants: Lee *et al.*Appl. Serial No.: 10/007,253
Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 13 of 34

$$(Y-39a) \qquad \qquad \begin{array}{c} H_2N \\ \\ R^9 \end{array}$$

,

Page 14 of 34

$$(Y-43a) \qquad \stackrel{H}{\underset{R^9}{\bigvee}} \qquad \stackrel{H}{\underset{N}{\bigvee}} \qquad \stackrel{H}{\underset{N}{\bigvee}} \qquad \qquad \stackrel{$$

$$(Y-45a)$$
  $\stackrel{N}{\longrightarrow}$   $\stackrel{N}{\longrightarrow}$  , and

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 15 of 34

Claim 79 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 71 wherein  $R^{22}$ ,  $R^{23}$ ,  $R^{25}$ , and  $R^{26}$  are each hydrogen.

Claim 80 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 71 which comprises the structure:

or a salt thereof.

Claim 81 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 80 in which L' is selected from:

—C=C-CH<sub>2</sub>— and

—C=C-CH<sub>2</sub>—O-CH<sub>2</sub>CH<sub>2</sub>—

Claim 82 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of claim 70 comprising the formula:

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 16 of 34

$$\begin{array}{c|ccccc}
R^{46} - L' - NUC \\
\hline
R^{24} & R^{23} & R^{22} & Y^1 & O \\
\hline
R^{24} & N & OH \\
\hline
R^{25} & R^{26} & S-Z
\end{array}$$

wherein:

 $[[Y^1]]$  <u>Y</u> is a rhodamine-type parent xanthene ring attached to the illustrated phenyl group at the xanthene C9 carbon;

 $R^{22}$ ,  $R^{23}$ ,  $R^{25}$ , and  $R^{26}$  are independently selected from hydrogen and (C<sub>1</sub>-C<sub>6</sub>) alkyl;

 $R^{24}$ , when taken alone, is  $(C_1-C_6)$  alkyl, or when taken together with  $R^{24}$  is  $(C_4-C_{10})$  alkyldiyl,  $(C_4-C_6)$  alkyleno,  $(C_4-C_6)$  heteroalkyldiyl or  $(C_4-C_6)$  heteroalkyleno;

 $R^{24}$ , when taken alone, is  $(C_1-C_6)$  alkyl, or when taken together with  $R^{24}$  is  $(C_4-C_{10})$  alkyldiyl,  $(C_4-C_6)$  alkyleno,  $(C_4-C_6)$  heteroalkyldiyl or  $(C_4-C_6)$  heteroalkyleno;

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 17 of 34

n is 1, 2, or 3;

S is sulfur;

Z is  $(C_1-C_{12})$  alkyl,  $(C_1-C_{12})$  alkyl substituted with one or more of the same or different W<sup>1</sup> groups,  $(C_5-C_{20})$  aryl, and  $(C_5-C_{20})$  aryl substituted with one or more of the same or different W<sup>2</sup> groups;

 $W^1$  is selected from -X, -R, =O, -OR, -SR, =S, -NRR, =NR,  $-CX_3$ , -CN, -OCN,

$$-SCN$$
,  $-NCO$ ,  $-NCS$ ,  $-NO$ ,  $-NO_2$ ,  $=N_2$ ,  $-N_3$ ,  $-S(O)_2O^-$ ,  $-S(O)_2OH$ ,  $-S(O)_2R$ ,  $-C(O)R$ ,

$$-C(O)X, -C(S)R, -C(S)X, -C(O)OR, -C(O)O^{-}, -C(S)OR, -C(O)SR, -C(S)SR,$$

-C(O)NRR, -C(S)NRR and -C(NR)NRR;

 $W^2$  is selected from -R, -OR, -SR, -NRR,  $-S(O)_2O^-$ ,  $-S(O)_2OH$ ,  $-S(O)_2R$ ,

$$-C(O)R, -C(O)X, -C(S)R, -C(S)X, -C(O)OR, -C(O)O^{-}, -C(S)OR, -C(O)SR, -C(S)SR,$$

-C(O)NRR, -C(S)NRR and -C(NR)NRR;

L is a selected from a bond,  $(C_1-C_{12})$  alkyldiyl,  $(C_1-C_{12})$  substituted alkyldiyl,  $(C_6-C_{26})$  arylalkyldiyl, -O-, -S-, -NR-, -C(O)O-, -C(O)NR-,  $-NRS(O)_2-$ , -NR-NR-, -NRC(O)O-, and -NRC(O)NR-;

R<sup>46</sup> is selected from -C(O)NR-, -C(O)O-, and -C(O)S,

L' is selected from  $(C_1-C_{20})$  alkyldiyl,  $(C_1-C_{20})$  heteroalkyldiyl,  $(C_1-C_{20})$  alkyleno,  $(C_1-C_{20})$  heteroalkyleno,  $(C_6-C_{26})$  arylalkyldiyl,  $(C_5-C_{20})$  heteroarylalkyldiyl, and substituted forms thereof; and

NUC is a nucleoside/tide or nucleoside/tide analog;

each R is independently selected <u>from</u> hydrogen,  $(C_1-C_6)$  alkyl,  $(C_5-C_{20})$  aryl,  $(C_6-C_{20})$  arylalkyl, and  $(C_6-C_{20})$  arylaryl; or when two R groups on the same nitrogen atom are taken together, those two R groups are  $(C_4-C_{10})$  alkyldiyl or  $(C_4-C_{10})$  alkyleno; and each X is independently a halogen.

Claim 83 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of Claim 82 in which  $[[Y^1]] \underline{Y}$  is selected from:

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 18 of 34

$$(Y-1b) \qquad R^{6} \qquad R^{5} \qquad R^{4} \qquad R^{9} \qquad R^{1} \qquad R^{2}$$

$$(Y-2b) \qquad \begin{array}{c} R^{14} \\ R^{15} \\ R^{13} \\ R^{12} \\ R^{11} \\ R^{10} \\ R^{8} \\ R^{9} \\ R^{1} \\ R^{21} \\ R^{20} \\ R^{18} \\ \end{array}$$

$$(Y-3b) \qquad \begin{array}{c} R^{15} \stackrel{R^{6'}}{\longrightarrow} R^{5} & R^{4} & R^{16} \\ R^{15} \stackrel{R^{6'}}{\longrightarrow} R^{5} & R^{4} & R^{16} \\ R^{17} \stackrel{R^{16}}{\longrightarrow} R^{17} & R^{17} & R^{18} & R^{18} \\ R^{18} \stackrel{R^{19}}{\longrightarrow} R^{1} & R^{18} & R^{18} & R^{18} \\ R^{19} \stackrel{R^{19}}{\longrightarrow} R^{18} & R^{18} & R^{18} & R^{18} \\ \end{array}$$

$$(Y-4b) \qquad R^{15} \stackrel{R^{6'}}{\longrightarrow} R^{5} \qquad R^{5} \qquad R^{4} \stackrel{\text{$\downarrow$}}{\longrightarrow} R^{16} \qquad R^{17} \qquad R^{18} \qquad R^{18}$$

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 19 of 34

$$(Y-1c) \qquad \qquad R^{6} \qquad \qquad R^{5} \qquad \qquad R^{3} \qquad \qquad R^{$$

(Y-3c) 
$$R^{15}$$
  $R^{6'}$   $R^{5}$   $R^{5}$   $R^{16}$   $R^{17}$ 

$$(Y-4c) \qquad R^{15} \stackrel{R^{6'}}{\longrightarrow} R^{5} \qquad R^{5} \qquad R^{16} \qquad R^{16} \qquad R^{17} \qquad R^{18} \qquad R$$

wherein the dashed line at the nitrogen or C4 atom indicates the point of attachment of L.

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 20 of 34

Claim 84 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 82 wherein:

an alkyldiyl or alkyleno bridge formed by taking R<sup>2</sup> together with R<sup>3</sup>, R<sup>4</sup> together with R<sup>3</sup>, R<sup>5</sup> together with R<sup>6</sup>, or R<sup>7</sup> together with R<sup>6</sup>, is ethano, propano, 1,1-dimethylpropano or 1,1,3-trimethylpropano; and

an aryleno bridge formed by taking  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  together or  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  together is benzo.

Claim 85 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 82 in which L is selected from phenyldiyl and naphthyldiyl.

Claim 86 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 82 in which L is  $-(CH_2)_i-\phi$ — where i is an integer from 1 to 6 and  $\phi$  is phenyldiyl or naphthyldiyl.

Claim 87 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 82 in which Z is selected from phenyl, benzyl, naphthyl, pyridyl and purinyl.

Claim 88 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of Claim 82 in which L'is L' is selected from: —C≡C—CH<sub>2</sub>— and —C≡C—CH<sub>2</sub>—O—CH<sub>2</sub>CH<sub>2</sub>—

Claim 89 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of

Claim 82 in which L' is:  $-C \equiv C - CH_2 - O - CH_2CH_2 - N - R^{48} - Wherein R^{47}$  is hydrogen or  $(C_1 - C_6)$   $(C_1 - C_5)$  alkyl, and  $R^{48}$  is selected from:

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 21 of 34

wherein each r is independently an integer from 1 to 6,  $R^{49}$  is hydrogen, (C<sub>1</sub>-C<sub>6</sub>) alkyl, or an amino acid side chain; and  $\phi$  is phenyldiyl or substituted phenyldiyl.

Claim 90 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 82 wherein  $R^{22}$ ,  $R^{23}$ ,  $R^{25}$ , and  $R^{26}$  are each hydrogen.

Claim 91 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of claim 82 in which  $[[Y^1]] \underline{Y}$  is selected from the group consisting of:

January 13, 2004 Page 22 of 34

January 13, 2004 Page 23 of 34

$$(Y-22b) \qquad \qquad \qquad \begin{matrix} H_2N & & & \\ & & & \\ & & & \\ & & & \end{matrix}$$

January 13, 2004 Page 24 of 34

Page 25 of 34

January 13, 2004 Page 26 of 34

January 13, 2004 Page 27 of 34

$$(Y-39b) \qquad H_2N \qquad Q \qquad N \qquad N \qquad N$$

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 28 of 34

wherein the dash at the nitrogen or C4 atom indicates the point of attachment of L.

Claim 92 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of Claim 82 which has the structure:

Page 29 of 34

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 30 of 34

Claim 93 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog

of Claim 92 in which L' is selected from: —C≡C-CH<sub>2</sub>— and

 $-C \equiv C - CH_2 - O - CH_2CH_2 - CH_2CH_2$ 

Claim 94 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 70 further comprising a donor dye or an acceptor dye whereby the rhodamine

dye and the donor dye or acceptor dye form an energy-transfer dye pair.

Claim 95 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog

of Claim 94 wherein the donor dye or acceptor dye is a fluorescein, rhodamine, cyanine,

phthalocyanine or squaraine.

Claim 96 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog

of Claim 94 wherein the donor dye or acceptor dye is 4'-aminomethyl-6-

carboxyfluorescein and the 4'-aminomethyl-6-carboxyfluoroscein is covalently attached

to the rhodamine dye by a linker.

Claim 97 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of

Claim 96 wherein the aminomethylfluorescein is further covalently attached by a linker

[[L]] L' to the nucleobase B of the nucleoside/tide or nucleoside/tide analog.

Claim 98 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog

of Claim 70 which is enzymatically incorporatable.

Claim 99 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog

of Claim 70 which is a terminator.

Claim 100 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog

Appl. Serial No.: 10/007,253 Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004 Page 31 of 34

of Claim 70 which is enzymatically extendable.

Claim 101 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 70 wherein R<sup>71</sup> and R<sup>70</sup> are hydrogen.

Claim 102 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 70 wherein R<sup>71</sup> and R<sup>70</sup> are hydroxyl.

Claim 103 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 70 wherein R<sup>71</sup> is hydroxyl, and R<sup>70</sup> is hydrogen.

Claim 104 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 70 in which nucleobase B is selected from adenine, 7-deazaadenine, cytosine, guanine, 7-deazaguanine, thymine and uracil.

Claim 105 (previously presented): A labeled polynucleotide or polynucleotide analog comprising a rhodamine dye conjugated to a nucleoside/tide or nucleoside/tide analog, wherein the rhodamine is a rhodamine-type parent xanthene having attached to the xanthene C9 carbon a phenyl group that is further substituted with an ortho carboxy or ortho sulfonate group or a salt thereof, one to three substituted or unsubstituted aminopyridinium groups and a substituted or unsubstituted alkylthio, or arylthio group.